REMARKS

Claims 1-49 are currently pending in this application. Claims 18, 19, 29-31 and 41-49 stand withdrawn. Claims 1, 20, 26, 27 and 36-38 are currently amended herein. Claims 2-11 and 14-16 are cancelled without prejudice or disclaimer as to the subject matter thereof. New claim 50 is presented for entry and consideration. Support for amended claims 1, 20, 26, 27 and 36-38 can be found throughout the application as originally filed, *inter alia*, on page 4, lines 26-34, on page 8, line 16 extending to page 9, line 16, as well as the claims as originally filed. Accordingly, Applicants respectfully submit that no new matter is introduced into the specification by way of the instant claim amendments.

Sequence Listing

In accordance with the provisions of 37 C.F.R. §§ 1.821 and 1.825, Applicants submit herewith a substitute paper copy of the substitute "Sequence Listing," totaling twenty-two (22) pages. Applicants also submit herewith a substitute computer readable copy of the substitute "Sequence Listing" on a CD-ROM in ASCII format as required by 37 C.F.R. §§ 1.821(e) and 1.825(a).

In accordance with the provisions of 37 C.F.R. § 1.821(f), the undersigned hereby states on information and belief that the content of the computer readable CD-ROM copy of the substitute "Sequence Listing" and the paper copy of the "Sequence Listing" submitted herewith are identical.

In accordance with the provisions of 37 C.F.R. § 1.825(a), the undersigned hereby states on information and belief that the content of the computer readable CD-ROM copy of the substitute "Sequence Listing" and the paper copy of the substitute "Sequence Listing" submitted herewith do not constitute new matter. The amendments included herein add entries for SEQ ID NOs: 86-89. The undersigned hereby states that the amendments provided herein have support in the application as filed, for example at page 7, lines 1-6, and the original sequence listing. Also, the amendment to the paper copy of the substitute "Sequence Listing," in accordance with 37 C.F.R. § 1.821(a) is accompanied by a substitute copy of the computer readable form including all previously submitted data with the amendment incorporated therein.

Applicants respectfully request entry of this sequence listing and submit that the sequence listing and amendment do not constitute new matter.

Examiner's Search Scope

Applicants note that the Office Action, on page 4, states that the search was extended to include SEQ ID NOs: 1, 2, 3, 4 and 5 as recited in claim 7. Furthermore, the Office Action states that the species of multi-epitope vaccine recited in claim 32 was also included for examination purposes. Applicants appreciate the Examiner's extension of the search to include SEQ ID NOs: 1, 2, 3, 4 and 5. Applicants also appreciate the Examiner's comment that SEQ ID NO:14 and SEQ ID NO:36 appear to be free of the prior art.

New Matter

The Office Action objected to the incorporation by reference to the parent applications. More specifically, the Office Action states that "[t]he amendment is not mentioned in the declaration or oath," and required cancellation thereof. Applicants respectfully submit that the amendment to the specification dated November 19, 2003, was submitted with the filing of the instant application and therefore should not be considered new matter. Applicants respectfully request clarification of this new matter objection.

Information Disclosure Statement

Applicants note the Office Action comments on page 4 regarding the listing of references in the specification. Applicants have compared the listing of references to the references submitted of record in the instant application, and believe that all references in the listing of references on pages 49-57 of the specification are currently of record and have been considered by the Examiner.

Applicants also note that page 34 of the Office Action states that reference 4 of the PTO Form 1449 filed 8/24/2004 has not been considered by the Examiner because it cannot be located in the parent application. Applicants re-submit herewith an IDS providing a copy of reference 4

from the original filing of 8/24/2004, and respectfully request review and an indication of consideration by the Examiner on the attached PTO SB/08 Form.

Objections

35 U.S.C. § 112, 1st paragraph, Enablement

The Office Action objected to the specification as allegedly failing to provide an enabling disclosure. More specifically, the Office Action states that the T2 cell line stably transfected with HLA-B35 and the W6/32 monoclonal antibody must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public.

a) Regarding the W6/32 monoclonal antibody, Applicants respectfully direct the Examiner's attention to the publication of Blok *et al.* (J. Immunol., 160:3437-3443 (1998)(attached herewith as Appendix A)), and specifically page 3438, 1st column, first full paragraph which states in pertinent part: "W6/32 hybridoma cells, producing anti-HLA class I mAb (IgG2a), were obtained from the American Type Culture Collection (ATCC)(Rockville, MD)." Applicants submit that this demonstrates the public availability of the W6/32 mAb producing hybridoma.

b) Regarding the T2 cell line stably transfected with HLA-B35, Applicants submit that the HLA-B35 amino acid sequence appears to be available under Genbank accession number AAB02169, while the complete coding sequence appears to be available under Genbank accession number D50299. The term "HLA assembly assay" may be more commonly known as the "HLA stabilization assay." The assembly assay is based on stabilization of the class I molecules after loading of peptide to the peptide transporter deficient cell line T2. The HLA stabilization wording is a well known term in the field of immunology and a skilled artisan understands that the technique involves using the transporter deficient T2 cell line and immunoprecipitation or FACScan flow cytometry for recovery. The method was described as early as 1993 by Nijman, H. W. *et al.*, Eur. J. Immunol. 23:1215-1219 (attached herewith as Appendix D). It appears that a cell line corresponding to that of Nijman *et al* was deposited in the ATCC under ATCC deposit number CRL-1992. Applicants submit that it is within the

abilities of a skilled artisan provided with the sequence of HLA-B35 to stably transfect said T2 cell line.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the objection to the specification as allegedly lacking an enabling disclosure.

Rejections

35 U.S.C. § 112, 1st paragraph, Enablement

Claims 1-7, 14-17, 20-28 and 32-40 were rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to provide enablement commensurate with the scope of the claims.

Applicants respectfully disagree and traverse this rejection.

Applicants appreciate the acknowledgement in the Office Action that the specification is enabling for SEQ ID NO:5. *See* Office Action, page 15, lines 2-3. It is well established under 35 U.S.C. §112 ¶ 1, that "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." (*United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1986)). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), MPEP § 2164.01.

Applicants submit that the specification provides adequate disclosure whereby one "reasonably skilled" in the art could make and use the claimed invention without undue experimentation. The specification provides at least three separate examples that are useful in guiding a skilled artisan to use the claimed invention. Example 1 presents an experiment in which cytotoxic T-lymphocyte (CTL) responses to survivin-derived peptide epitopes were evaluated using either patients suffering from a form of cancer or healthy individuals. In Example 1, which sets forth the methodology involved in the example, it is noted that SEQ ID NO: 1, SEQ ID NO:4 and SEQ ID NO:5 each provided binding to HLA-A2. It is noteworthy that the SEQ ID NO:4 and SEQ ID NO:5 "peptides bind with almost similar high affinity to HLA-A2 as the positive control." See Specification, page 25, lines 13-16.

Example 2 and Example 5 further evaluated responses to survivin-derived peptide epitopes. It is noted that for purposes of amended claim 1 that Example 2 and Example 5 evaluated SEQ ID NO:5 (encompassed by amended claim 1), and that the Office Action has acknowledged enablement for SEQ ID NO:5. Nonetheless, the methodology of Example 2 and Example 5 are equally applicable to the remaining SEQ ID NOs encompassed by amended claim 1.

Applicants submit herewith a declaration under 37 C.F.R. § 1.132 of Dr. Mads Hald Andersen (attached herewith as Appendix C), a named inventor. In the declaration, Dr. Andersen states that "[t]he clinical relevance of using Sur1M2 peptide in cancer immunotherapy is demonstrated in Example 5 of the application." It is Dr. Andersen's opinion that "the clinical relevance of using the other peptide species in cancer therapy is supported by the fact that in relation to the subject survivin tumor associated-antigens it is not possible to identify a single dominant epitope peptide. In addition, the inclusion of more peptide species may provide for the targeting of multiple HLA alleles/molecules."

Regarding the Reker *et al* reference, Dr. Andersen explains that the "statement was presented in the discussion of the research data, not to express concerns with respect to the relevance of using survivin peptides in cancer immunotherapy, but merely to indicate that phase III clinical trials - the only firm proof that a vaccine works - had not yet been completed."

It is also noted that the Office Action states that "[t]he specification does not disclose the sequence of survivin, nor does it incorporate by reference the disclosure of U.S. Pat. No. 6,245,523 into the instant specification, ..." Applicants respectfully direct the Examiner's attention to page 3, lines 14-16 of the specification as originally filed in which it is stated "[t]he survivin protein and the potential diagnostic and therapeutic use hereof are disclosed in ... US 6,245,523, which are incorporated herein by reference."

In light of the instant amendments and remarks provided herein, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 17, 20-28 and 32-40 under 35 U.S.C. § 112, 1st paragraph. Applicants note that rejected claims 2-7 and 14-16 are cancelled herein without prejudice or disclaimer.

35 U.S.C. § 112, 1st paragraph, Written Description

Claims 1-6, 14-17, 20-28 and 32-40 were rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the written description requirement for substantially the same reasons as set forth in the enablement rejection above. For the same reasons discussed above with regards to the enablement rejection, and in light of the instant amendments and remarks provided herein, Applicants respectfully request reconsideration and withdrawal of this written description rejection.

35 U.S.C. § 112, 2nd paragraph

a) Claim 1 was rejected as indefinite in the recitation of "... as determined by the assembly binding assay as described herein". Applicants submit that this rejection has been rendered moot by way of claim amendment, and respectfully request reconsideration and withdrawal of the rejection of claim 1 as indefinite.

b) Claim 20 was rejected as indefinite in the recitation of "[a] peptide ... comprising, for each specific HLA allele, any of the amino acid residues as indicated in the following table ..." Applicants submit that this rejection has been rendered moot by way of claim amendment, and respectfully request reconsideration and withdrawal of the rejection of claim 20 as indefinite.

c) Claim 24 was rejected as indefinite in the recitation of "... the breast cancer cell line MCF-7 and the melanoma cell line FM3." Applicants submit that the recitation of breast cancer cell line MCF-7 and melanoma cell line FM3 is not indefinite, as these are art recognized cell lines. For example, breast cancer cell line MCF-7 is commercially available from the LGC Promochem / ATCC as ATCC Number HTB-22TM. (*See* http://www.lgcpromochem-atcc.com/common/catalog/numSearch/numResults.cfm?atccNum=HTB-22). Regarding the melanoma cell line FM3, Dr. Andersen states in his declaration that "[t]he cell line was originally described by Kirkin et al (Cancer Immunol Immunother, 41:71-81 1995) and is well recognized within the art."

d) Claim 27 was rejected as indefinite in the recitation of "... peptide ... having the sequence contained in SEQ ID NO:36 ... peptide having the sequence contained in SEQ ID NO:14." Applicants submit that this rejection has been rendered moot by way of claim amendment, and respectfully request reconsideration and withdrawal of the rejection of claim 27 as indefinite.

e) Claims 36 and 37 were rejected as indefinite in the recitation of "... diagnosis of the presence in a cancer patient of survivin reactive T cells." Applicants submit that this rejection has been rendered moot by way of claim amendment, and respectfully request reconsideration and withdrawal of the rejection of claims 36 and 37 as indefinite.

Prior Art Rejections

As an initial matter, Applicants respectfully address the characterization of both of the cited Andersen references as prior art. Applicants submit that their priority filing (U.S. provisional patent application no. 60/352,284) was filed on January 30, 2002, and includes disclosure of SEQ ID NO:1, SEQ ID NO:4 and SEQ ID NO:5.

Applicants further submit that both Andersen references were published less than one year prior to the filing of Applicants' provisional patent application. It is noted that one of the Andersen references (Cancer Research, 61:869-872) (attached herewith as Appendix E) appears to have been published with the incorrect publication date of February 1, 2000, on the front page. Applicants submit that this is in error, as the text at the bottom of the left-hand column on the first page states that the manuscript was not even submitted until August 14, 2000, and was not accepted for publication until December 7, 2000, more than 10 months after the erroneous publication date. Furthermore, Applicants submit (attached herewith as Appendix B) a copy of the on-line Table of Contents for Volume 61, Issue 3 (2001), of Cancer Research. This Table of Contents clearly identifies the relevant Andersen reference on page 3, 5th reference of the attached on-line Table of Contents in Appendix B. Because Applicants' provisional application was filed less than one year after the publication of the two Andersen references, Applicants submit that the Andersen references are not prior art under 35 U.S.C. § 102(b).

Furthermore, Applicants submit herewith a declaration under 37 C.F.R. § 1.132 by inventor Mads Hald Andersen (attached as Appendix C), in which Dr. Andersen sets forth the contribution of each of the non-inventor and inventor authors of the two cited Andersen publications. Applicants submit that the declaration of Dr. Andersen establishes that the cited Andersen *et al* articles are describing Applicants' own work.

35 U.S.C. § 102 (b)

a) Claims 1-7, 14-17, 20-24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of Andersen *et al* (Cancer Res., 2000, 61:869-872) as evidenced by Andersen *et al* (Cancer Res., 2001, 61:5964-5968).

Applicants respectfully disagree and traverse this rejection.

As discussed above, Applicants believe that neither of the cited Andersen *et al* references is prior art under 35 U.S.C. § 102 (b) to the claimed invention for the reasons provided. Furthermore, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* articles are describing Applicants' own work. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims -7, 14-17, 20-24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b).

b) Claims 1-7, 14-17, 20-24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of Andersen *et al* (Cancer Res., 2001, 61:5964-5968).

Applicants respectfully disagree and traverse this rejection.

As discussed above, Applicants believe that neither of the cited Andersen *et al* references is prior art under 35 U.S.C. § 102 (b) to the claimed invention for the reasons provided. Furthermore, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* article is describing Applicants' own work. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims -7, 14-17, 20-24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b).

c) Claims 1-7, 14-17, 20-24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of Schmitz *et al* (Cancer Res., 2000, 60:4845-4849) as evidenced by Andersen *et al* (Cancer Res., 2001, 61:5964-5968).

Applicants respectfully disagree and traverse this rejection.

As stated in MPEP § 2131, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicants submit that the disclosure of Schmitz *et al* fail to teach all of the claimed elements. For example, Schmitz *et al* fail to teach any of SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:14. As noted previously, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* article is describing Applicants' own work. As Schmitz *et al* do not teach all of the elements of the rejected claims as amended herein, Schmitz *et al* do not anticipate the subject matter of the rejected claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-7, 14-17, 20-24, 36 and 38-40 under 35 U.S.C. § 102 (b).

d) Claims 1-3, 15-17, 22-25, 28 and 32-36 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of International Publication No. WO 00/03693.

Applicants respectfully disagree and traverse this rejection.

As stated in MPEP § 2131, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicants submit that the disclosure of International Publication No. WO 00/03693 fails to teach all of the claimed elements. For example, International Publication No. WO 00/03693 fails to teach any of SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:14. As International Publication No. WO 00/03693 does not teach all of the elements of the rejected claims as amended herein, International Publication No. WO 00/03693 does not anticipate the subject matter of the rejected claims. Accordingly, Applicants respectfully request

reconsideration and withdrawal of the rejection of claims 1-3, 15-17, 22-25, 28 and 32-36 under 35 U.S.C. § 102 (b).

35 U.S.C. § 103(a)

a) Claims 1-7, 14-17, 20-25 and 36-40 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Andersen *et al* (Cancer Res., 2000, 61:869-872) in view of Campbell and U.S. Patent No. 6,572,864.

Applicants respectfully disagree and traverse this rejection.

Applicants submit that the prior art reference (or references when combined) must teach or suggest all the claim elements in order to render the claimed subject matter obvious. Applicants respectfully submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* article is describing Applicants' own work. Applicants submit that the remaining references, alone or in combination, fail to teach or suggest all of the claim elements. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-7, 14-17, 20-25 and 36-40 were rejected under 35 U.S.C. § 103(a).

b) Claims 1-7, 14-17, 20-25 and 36-40 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Andersen *et al* (Cancer Res., 2001, 61:5964-5968) in view of Campbell and U.S. Patent No. 6,572,864.

Applicants respectfully disagree and traverse this rejection.

Applicants submit that the prior art reference (or references when combined) must teach or suggest all the claim elements in order to render the claimed subject matter obvious. Applicants respectfully submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* article is describing Applicants' own work. Applicants submit that the remaining references, alone or in combination, fail to teach or suggest all of the claim elements. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-7, 14-17, 20-25 and 36-40 were rejected under 35 U.S.C. § 103(a).

c) Claims 1-7, 14-17, 20-25 and 36-40 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Schmitz *et al* (Cancer Res., 2000, 61:869-872) in view of Campbell and U.S. Patent No. 6,572,864.

Applicants respectfully disagree and traverse this rejection.

Applicants submit that the prior art reference (or references when combined) must teach or suggest all the claim elements in order to render the claimed subject matter obvious. Applicants submit that none of the cited references, alone or in combination, teaches or suggests all of the claim elements. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-7, 14-17, 20-25 and 36-40 were rejected under 35 U.S.C. § 103(a).

d) Claims 1-3, 14-17, 22-25 and 32-37 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over the disclosure of International Publication No. WO 00/03693 in view of U.S. Patent No. 6,572,864.

Applicants respectfully disagree and traverse this rejection.

Applicants submit that the prior art reference (or references when combined) must teach or suggest all the claim elements in order to render the claimed subject matter obvious. Applicants submit that neither of the cited references, alone or in combination, teaches or suggests all of the claim elements. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-3, 14-17, 22-25 and 32-37 were rejected under 35 U.S.C. § 103(a).

e) Claims 1-6, 14-17, 20-25 and 32-36 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over the disclosure of International Publication No. WO 00/03693 in view of Rammensee *et al.*

Applicants respectfully disagree and traverse this rejection.

Applicants submit that the prior art reference (or references when combined) must teach or suggest all the claim elements in order to render the claimed subject matter obvious. Applicants submit that none of the cited references, alone or in combination, teaches or suggests all of the claim elements. Accordingly, Applicants respectfully request reconsideration and

withdrawal of the rejection of claims 1-6, 14-17, 20-25 and 32-36 were rejected under 35 U.S.C. § 103(a).

CONCLUSION

An indication of allowance of all claims is respectfully solicited. Early notification of a favorable consideration is respectfully requested.

Respectfully submitted,

HUNTON & WILLIAMS LLP

Date: September 24, 2007

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